

test compounds. Dr. Clark points out that the tissue from the animal treated with the piperidino compound--Exhibit 5--shows little if any stimulation of the epithelial cells, whereas the section from the pyrrolidino-treated animal--Exhibit 6--shows rather extensive stimulation of the epithelial cells.

Declaration of Blake L. Neubauer, Ph.D.

Dr. Neubauer carried out tests in male guinea pigs. It is noted that, in these tests, the piperidino compound of this invention was tested as the hydrochloride salt, and the pyrrolidino compound was the free base. The data are presented, despite the difference in form of the compounds, because they are the only available results of testing the compounds in male guinea pigs. The results indicated to Dr. Neubauer that neither compound has an estrogenic effect in the animals.

Dr. Neubauer also studied and analyzed data from Mr. Black's tests 953 and 954, and also supervised analyses for DNA, RNA, protein and water of tissues from those animals. He initiated a statistical analysis of the data and presents his conclusions. Dr. Neubauer concludes that the pyrrolidino compound produced a significant increase in the normalized uterine weight (that is, the uterine weight adjusted for body weight) and in the uterine water content compared to the measurements on animals treated with the piperidino compound of this invention. He therefore concludes that the difference in uterine growth is more likely attributable to alterations in water content than to changes in tissue nucleic acid or protein.

Conclusion

Applicant has presented an amendment which is responsive to the rejection of Claims 48-62 and makes that rejection moot.

Applicant submits herewith five Declarations by expert physiologists who have tested the compound of the present invention. The factual results presented in the Declarations show that the present invention is unexpectedly different from and superior to the pyrrolidino compound which is the reference's species closest to the present invention. Accordingly, Applicant has shown that the present invention, when considered as a whole including its properties, is unexpectedly superior to the art, and Applicant accordingly requests reconsideration and withdrawal of the rejection under 35 U.S.C. 103.

Respectfully submitted,



Joseph A. Jones
Attorney for Applicant
Registration No. 26,472

Phone: 317-261-3474

Eli Lilly and Company
Patent Division/JAJ
307 East McCarty Street
Indianapolis, Indiana 46285

12 Nov. 1982